REMARKS

Claim Objection

Claim 19 is objected to under 37 CFR 1.75(c) for failing to further limit the subject matter of claim 17. Applicants submit that claim 17, as amended, is drawn to a vector *comprising*, among other nucleic acid sequences, a nucleic acid sequence coding for a T-DNA, including a right border, RB, and a left border, LB, which permit the vector to function as a binary plasmid. Claim 17 *does not require* an expression promoter and/or a transcription terminator to be situated between the left border and the right border of the T-DNA. Claim 19, as the Examiner points out, provides an additional structural requirement which is not recited in claim 17: "a nucleic acid sequence corresponding to at least one expression promoter and a nucleic acid sequence corresponding to at least one transcription terminator situated between the left border, LB, and the right border, RB, of the T-DNA." This additional element narrows the scope of vector in claim 19 by further defining the position of the promoter and terminator, i.e., between the borders of the T-DNA sequence. Therefore, claim 19 does further limit the subject matter of claim 17 from which claim 19 depends. Applicants respectfully request the objection on claim 19 be withdrawn.

Claim Rejections – 35 USC §112, Second Paragraph

Claims 19-24 are rejected under 35 USC §112, second paragraph as allegedly being indefinite for the recitation of "coding" in "a nucleic acid sequence coding for at least one expression promoter and at least one transcription terminator." Applicants have amended claim 19 to recite "a nucleic acid sequence corresponding to at least one expression promoter and a nucleic acid sequence corresponding to at least one transcription terminator". Claims 20-24 depends from claim 19. Applicants believe the above amendment in claim 19 obviates the §112 second paragraph rejections on claims 19-24.

Claims 21 and 22 are rejected as allegedly being indefinite for the recitation of "where said expression promoter is a plant expression promoter" because it is "unclear whether it means a promoter functions in a plant or isolated from a plant gene." Claims 23 and 24 are similarly

rejected for the recitation of "wherein said transcription terminator is a terminator of a plant cell" because it is "unclear whether it is a terminator isolated from a plant gene or a terminator functions in a plant." Applicants submit that the term "plant promoter" is defined in the present specification as "a promoter capable of initiating transcription in plant cells." (page 2, lines 25-26) It is therefore clear that such plant promoter does not have to be one isolated from a plant gene as long as it is "capable of initiating transcription in plant cells." Similarly, a terminator of a plant cell is a terminator "functional" in plant cells and does not have to be one isolated from a plant gene (e.g., see page 6, lines 14-15). Therefore, claims 21-22 and claims 23-24 are not indefinite for their recitation of "plant expression promoter" and "a terminator of a plant cell", respectively. For the sole purpose of expediting the examination of the present application, however, Applicants have amended the claims 21 and 23 to recite "functions in a plant" with respect to the promoter and the terminator.

In view of the above amendments and remarks, Applicants respectfully request the §112 second paragraph rejections on claims 19-24 be withdrawn.

Claim Rejections – 35 USC §103(a)

Claims 17-24 are rejected under 35 USC §103(a) as allegedly being obvious over Thomashow et al., in view of Valla et al. The Examiner states that Thomashow et al. teach a binary vector pMEN020 "*comprising* [an] origin of bacterial replication ori-322, a vegetative origin of replication ori-V, the left border of T-DNA, a chimeric gene as selection marker..., right border of T-DNA and bacterial spectinomycin resistance gene.... [This] plasmid does not contain vir gene encoding proteins essential for the transfer and integration of the target gene inserted in the T-DNA region.... [This] plasmid requires the trfA gene product to replicate in Agrobacterium.... Thomashow teach a strain of Agrobacterium comprising a modified Ti plasmid encoding trfA gene as a helper vector the pMEN020 vector to replicate in Agrobacterium." The Examiner acknowledges that Thomashow et al. does not teach a vector comprising elements of pMEN020 and trfA gene on the same vector. However, the Examiner states that Valla et al. teaches vectors "comprising trfA gene in cis and trans from RK2 origin," and "the temperature sensitive phenotype is influenced by copy number of the trfA transcripts, wherein the cis vectors are low copy number and trans vectors are high copy number." The

Examiner concludes that, because of the combination teaching of Thomasshow et al. and Valla et al., it would have been obvious to one of ordinary skill of art to make a synthetic binary vector comprising elements of the pMEN020 vector and further comprising the trfA locus in cis position and to manipulate the vectors comprising trfA in cis or trans position to change the activity of temperature sensitive mutants of trfA.

Applicants respectfully disagree with the 103(a) rejections. Applicants submit that claim 17 and its dependent claims 18-24 of the present invention are drawn to a synthetic vector comprising a nucleic acid sequence for a first origin of replication; - a nucleic acid sequence coding for a selection agent; - a trfA locus coding for a protein that permits an increase in the replication rate of the vector; and - a nucleic acid sequence coding for a T-DNA, including a right border, RB, and a left border, LB, which permit the vector to function as a binary plasmid. It is clear *the trfA locus is on the same synthetic vector which carries the T-DNA*.

No teaching or suggestion of the present invention

Neither Thomashow et al. nor Valla et al. teaches or suggests a single vector containing both trfA locus and T-DNA.

Thomashow et al. teaches a transformed plant that comprises one or more environmental stress tolerance genes. The plasmid pMEN020 is used to transform the plant cells. Thomashow et al. teaches that the pMEN020 vector "is a binary cloning vector that contains both *E. coli* and *Agrobacterium tumefaciens* origins of DNA replication but no vir genes encoding proteins essential for the transfer and integration of [the desired T-DNA]" (see column 27, lines 54-58). Even without the benefit of Valla et al., it is apparent that the authors of Thomashow et al. were aware that pMEN020 is only able to replicate in *Agrobacterium* in combination with a specific Ti shuttle plasmid containing the trfA gene from an *Agrobacterium* strain (e.g., column 27, lines 58-63; column 28, lines 5-7). Yet, instead of cloning trfA gene onto pMEN020, the authors used a trfA helper strain to achieve the purpose of replicating pMEN020. There is no teaching or suggestion in Thomashow et al. to have the trfA gene expressed from the same binary vector pMEN020. Valla et al. teaches the isolation and the characterization of trfA temperature sensitive (ts) mutants for replication in *E. coli*. Valla et al. does not even mention the construction of a binary vector that functions in plant. The authors constructed two plasmids for

the purpose of isolating mutants in the trfA gene and for analyzing the properties of the trfA proteins. They concluded that when the mutant trfA genes were present in trans position, three of the four mutants could withstand all temperature tested, however, activity was reduced compared to the wild type. The problems related to temperature sensitivity do not indicate in any way as to how to construct the synthetic vectors of the present invention.

MPEP § 2142 states that the teaching or suggestion to make the claimed combination, i.e., a plant binary vector carrying the trfA gene, must be found in the prior art and not based on applicants' disclosure. There is no such teaching or suggestion found in either Valla et al. or Thomashow et al.

No motivation to combine

"The mere fact that reference *can* be combined or modified does not render the resultant combination obvious *unless* the prior art also suggests the *desirability* of the combination." (MPEP 2143.01, citing *In re Mills,* 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990)).

In addition to the lack of teaching or suggestion of having the trfA gene on the same binary vector, as recited in the claims of the present invention, there would be no motivation for one skilled in the art to combine the teaching on trfA gene in Valla et al. and the teaching of a binary vector of Thomashow et al. As discussed herein above, the requirement of the trfA gene for a replicable binary vector is known to the authors of Thomashow et al., yet they chose to use a helper strain carrying the trfA gene, instead of cloning the trfA gene onto pMEN020 to achieve this goal. As indicated in Thomashow et al., the helper strain is a strain well characterized in the literature and in U.S. Patent Nos. 5,773,701 and 5,773,696, and is readily available (see, column 27, line 59 to column 28, line 5). The successful application of pMEN020 as a plant binary vector, with the assistance of the helper strain carrying trfA gene would only reduce the desire of one skilled in the art to make a binary vector carrying the trfA gene itself. In other words, Thomashow et al. would not provide motivation for one with ordinary skills in the art to combine the trfA gene taught by Valla et al. and the binary vector taught by Thomashow et al. In fact, the authors in Thomashow et al. were not motivated to combine such teachings themselves, due to the availability of the helper strain carrying the trfA gene. One skilled in the art, by following

the teachings of Thomashow et al. would likely use the same strategy of using an available helper strain to make a binary vector replicable in *Argrobacterium*.

No reasonable expectation of success

There is no reasonable expectation of success in making a replicable binary vector by replacing the helper strain used in Thomashow et al. with a trfA gene cloned onto the same binary vector, as recited in claims 17-24 of the present invention.

Thomashow et al. teaches the following with respect to the helper strain:

> "The recipient ABI strain of Agribacterium carries a modified defective Ti plasmid that serves as a helper plasmid containing a complete set of vir genes but lacks portions or all of the T-DNA region. ABI is the A208 Agrobacterium tumefaciens strain carrying the disarmed pTiC58 plasmid pMP90RK (Koncz et al. Mol. Gen. Genet. 204:383-396 (1986)). The disarmed Ti plasmid provides the trfA gene functions that are required for autonomous replication of the binary vectors after transfer into the ABI strain. When plant tissue is incubated with the ABI::binary vector strains, the vectors are transferred to the plant cells by the vir functions encoded by the disarmed pMP90RK Ti plasmid. After the introduction of the binary vector into the recipient Agribacterium, the vir gene products mobilize the T-DNA region of the pMEN020 plasmid to insert the target gene, e.g. the gene encoding the regulatory binding protein, into the plant chromosomal DNA, thus transforming the cell" (column 27, line 66 to column 28, line 15).

Although the above paragraph teaches that the tfrA gene is required for the replication of the binary vector in Agrobacterium, nothing in Thomashow et al. indicates the tfrA gene alone, absent of other components that may be provided by the helper strain, would be sufficient to make the binary vector replicable. Valla et al., not teaching binary vector at all, does not teach whether the trfA gene alone is sufficient in making a binary vector replicable in Agrobacterium either.

According to MPEP 2142, the reasonable expectation of success must be found in the prior art, and not based on applicants' disclosure. Absent the teaching of the present invention, there would be no basis to assume that by cloning the trfA gene onto a binary vector would achieve the same function that the helper strain used in Thomashow et al. could achieve. Therefore, there would be no reasonable success to use the present invention as claimed in claims 17-24 based on the teaching of Thomashow et al. and Valla et al.

In view of the above, Applicants submit that claims 17-24 are not obvious over Thomashow et al., in view of Valla et al. Applicants respectfully request the withdrawn of the 103(a) rejections on claims 17-24.

New claims 56-57

Currently added claim 56 are drawn to a synthetic vector comprising - a nucleic acid sequence coding for a first origin of replication; - a nucleic acid sequence coding for a selection agent; - a trfA locus coding for a protein that permits an increase in the replication rate of the vector; and - a nucleic acid sequence coding for a T-DNA, including a right border, RB, and a left border, LB, which permit the vector to function as a binary plasmid, *wherein the nucleic acid sequence coding for a selection agent is located near the left border of the T-DNA.*

Claim 56 is supported throughout the specification, e.g., on pages 5-8. With respect to the limitation of the selection agent located near the left border, the specification teaches:

> "In addition, [the vectors of the present invention] can have *a selection cassette near the left border*, as well as rare restriction sites in their «polylinkers» (multiple cloning sites)." (page 10, lines 5-7, *emphasis added.*)

Applicants recognizes that there may be potential problems of having the selection agent near the right border and there are advantages of having the selection agent locate near the left border of the T-DNA over having the selection agent near the right border of the T-DNA (see, page 1, lines 22-31). The right border of T-DNA gets cleaved during T-DNA processing (see Ziemienowicz, 2001, *Odyssey of Agrobacterium T-DNA*, Acta Biochi. Polo.: 623-635 Exhibit A). Based on the transferring mechanism taught in Ziemienowicz, there may be problems inherent with the preferential right to left border transfer of T-DNA and improves the chances of having the gene of interest transferred to the plant cell in cells expressing the selectable marker gene. The design of the present invention as recited in claim 56, i.e., the selection agent located near the left border, overcomes potential difficulty of maintaining the selection agent.

As discussed above for claims 17-24, claim 56 is not obvious over Thomashow et al. and Valla et al. In addition, neither Thomashow et al. nor Valla et al. teaches the additional

limitation of claim 56, i.e., wherein the nucleic acid sequence coding for a selection agent is located near to the left border of the T-DNA.

Currently added claim 57 is drawn to a vector comprising a nucleic acid sequence selected from the group consisting of SEQ ID Nos. 01-22.

Claim 57 is supported throughout the present specification, e.g., on page 8. Neither Thomashow et al. nor Valla et al. teaches the limitation of claim 56, i.e., a nucleic acid sequence selected from the group consisting of SEQ ID Nos. 01-22.

Therefore, new claims 56 and 57 are supported by the present specification and is patentable over Thomashow et al. and Valla et al.

Applicants submit that all claims, i.e., claims 17-24, and 56-57, are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

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